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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/855,316	05/15/2001	Jacqueline Sharon	701586-46074 DIV 2	9999
26770	7590	02/26/2004	EXAMINER	
NIXON PEABODY LLP ATTENTION: DAVID RESNICK 101 FEDERAL STREET BOSTON, MA 02110			YAEN, CHRISTOPHER H	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/855,316	Applicant(s) SHARON, JACQUELINE	
	Examiner Christopher H Yaen	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 November 2003.
2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 111,112,114-121 and 123-131 is/are pending in the application.
 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 111,112,114-116,118-121 and 123-131 is/are rejected.
7) ☒ Claim(s) 117 is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/2003 has been entered.
2. Claims 124-131 are newly added, claims 1-110, 113, and 122 are canceled without prejudice or disclaimer
3. Claims 111-112, 114-121, and 123-131 are therefore pending and examined on the merits.

New Arguments

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 111-112, 114-116, 118, 120-121, and 126-131 are rejected under 35 U.S.C. 102(b) as being anticipated by Gram *et al* (PNAS USA 1992 April;89:3576-3580). The claims of the instant invention are interpreted as follows: a composition

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comprising a mixture of expression vectors that comprise V_H and V_L regions (which constitutes a pair of variable regions) that are associated with each other and form a domain, wherein the mixture of expression vectors are generated by transferring nucleic acid segments from one vector into another, so as to generate a mixture of expression vectors that encode a diverse array of V_H and V_L regions. Because antibody variable domains can in essence act as receptors for antigens, the term "receptor" will be interpreted as any antibody variable chain fragment.

Gram *et al* disclose an in vitro selected and affinity matured antibody fragment derived from an antibody phage library derived from bone marrow cells. Gram *et al* disclose the construction of a first vector comprising a nucleic acid sequence encoding heavy and light chain variable regions from a diverse population of B-cells (see page 3577 under "**Naïve Immunoglobulin μ / κ Library Construction**"). Furthermore, Gram *et al* teaches that the sequences that are cloned into said first vector are then excised and sub-cloned into a second vector (ScpComb3) through the digestion of the first vector with two specific restriction endonucleases that digests the diverse population of nucleic acid sequences for "in-mass" transfer into the second vector. Prior to the said "in-mass" transfer, Gram *et al* discloses that the diverse population of sequence or "library" of sequences are panned and selected (see page 3577 under "**Panning**" and "**Colony Screening of Panned Libraries**"), and that vectors are phages (see page 3577 under "**Panning**"). Because the USPTO do not have the facilities to determine whether the selection process, has reduced the population of the expression library to less than 10%, in the absence of evidence to the contrary, Gram *et al* during their

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Panning and affinity maturation process were able to reduce said library to less than 10%.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 111-112, 114-116, 118-121, 123-131 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gram *et al* in view of Bender *et al* (Hum Antibodies Hybridomas 1993 Apr;4(2):74-79). See above for Gram *et al* teachings. Gram *et al* do not specifically characterize their expression vectors to the extent that the vectors comprise a variable region derived from one species and a constant region from antoehr species, nor do they discuss the use of constant regions in their second vector. This deficiency is made up by Bender *et al*, wherein it is disclosed that the fusion of library derived antibody fragments to Fc regions are generated making full length and functionally active whole antibodies.

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to make a composition of expression vectors wherein the vectors comprise nucleic acid sequence that encode pair of variable regions and further comprising genes that encode constant regions so as to generate a diverse population of expression vectors that are able to express whole or full length antibodies. One of

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skill in the art would have been motivated to do so because Gram *et al* teach that expression vectors comprising diverse variable regions can be generated and screened, while Bender *et al* states that variable regions derived from teachings similar to Gram *et al* could be further improved by the addition of the constant regions. Bender *et al* provide further motivation to add the constant regions because it is stated by Bender *et al* that antibody fragments tend to have short half life in circulation and that the addition of the constant region of Fc portion of the antibody would improve circulation and half-life and antibody effector function (see page 75 1st paragraph). One of skill in the art would have also expected a reasonable amount of success in combining the references because Bender *et al* successfully generated whole antibody by combining nucleic acid sequence encoding antibody fragments generated from antibody libraries to constant region genes.

Conclusion

8. Claim 117 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
February 21, 2004

GARY NICKOL
PRIMARY EXAMINER

